

## REMARKS

Claims 1-49 are pending and under examination. Claims 1, 6-10, 17, 33, 38 and 44 have been amended. Claim 15 has been canceled. Support for the amendments can be found throughout the specification and the claims as filed. In particular, support for the amendment to claim 1 can be found in original claim 15. Claims 6-10 have been amended to correct antecedent basis. Claim 17 has been amended to reflect antecedent basis for amended claim 1. Support for the amendment to claim 33 can be found, for example, on page 26, lines 13-28, page 27, lines 16-29, and Figures 5A and 5B. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Applicants appreciate the indication by the Examiner that claims 15 and 17 are allowable. Claim 1 has been amended to incorporate the limitations of claim 15. All the remaining claims are dependent from claim 1 or its dependents. Accordingly, Applicants respectfully submit that all claims should be considered allowable, as discussed more specifically below.

### Regarding the Priority Claim

The Office Action indicates that Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120. The Office Action indicates that the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application, 60/258,621, and that the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of 35 U.S.C. § 112, first paragraph.

Applicants respectfully traverse the indication that Applicants are not entitled to priority to parent provisional application 60/258,621, filed December 21, 2000. Firstly, the present application contains subject matter clearly disclosed in priority provisional application 60/258,621. In particular, the parent provisional application describes methods of studying protein surfaces using NMR by Solvent Exposed Amides (SEA) with TROSY, referred to therein as "SEA-TROSY," and as described in the present application. In addition, Figures 1a and 1b of the priority application are the same as Figures 2a and 2b, respectively, of the present application.

Secondly, Applicants respectfully submit that the priority provisional application provides sufficient description and guidance to comply with the requirements of 35 U.S.C. § 112, first paragraph. Applicants contend that the specification of priority provisional application 60/258,621 provides sufficient description and guidance to satisfy the requirements of 35 U.S.C. § 112, first paragraph, for the disclosure therein. Furthermore, the Office Action sets forth no basis for denying priority to provisional application 60/258,621. Accordingly, Applicants respectfully request that the present application be afforded priority to provisional application serial No. 60/258,621, filed December 21, 2000, and provisional application serial No. 60/263,475, filed January 22, 2001, as properly claimed in the first paragraph of the specification of the present application.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 1-10 and 33-49 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed. Applicants respectfully submit that the claims are clear and definite.

With respect to claim 1, the Office Action indicates that the term “demagnetizes” in part (c) is vague and indefinite because it is allegedly unclear if the pulse sequence demagnetizes the protons of the macromolecule or whether the protons of the macromolecule are still magnetized “with a different magnetization than that of the second proton.” Claim 1 step (c) recites that the sample is irradiated “with a pulse sequence that preferentially demagnetizes the protons of the macromolecule relative to the second proton.” Thus, the claim clearly recites that the pulse sequence preferentially “demagnetizes the protons” of the macromolecule “relative to the second proton.” Furthermore, the specification describes and illustrates such a step on page 11 and Figure 1. Figure 1a illustrates a macromolecule and second molecule, as in step (a) (page 11, lines 1-8). Figure 1b illustrates applying a magnetic field to the sample and magnetizing the first proton of the macromolecule and the second proton of the second molecule, as in step (b) (page 11, lines 9-12). Figure 1c illustrates irradiating the sample with a pulse sequence that preferentially demagnetizes protons of the macromolecule relative to the second proton of the second molecule, as in step (c) (page 11, lines 12-15). Applicants respectfully submit that, based on the clear language in the claim and the teachings in the specification, one skilled in the art would understand the meaning of the

term “demagnetizes,” as recited in claim 1 step (c). Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claim 6 is alleged to be indefinite for the term “polypeptide” because there is insufficient antecedent basis for this term. Claim 6 has been amended to depend from claim 2, which recites the term “polypeptide,” as suggested by the Examiner. Accordingly, it is respectfully submitted that this claim is clear and definite.

Claims 7-10 are alleged to be indefinite for the phrase “the amino acids of the protein” because this phrase lacks antecedent basis. Claims 7-10 have been amended to recite the term “polypeptide” and to depend from claim 2, which also recites the term “polypeptide.” Accordingly, it is respectfully submitted that this claim is clear and definite.

Claims 33, 38 and 44 are alleged to be indefinite in that it is allegedly unclear whether the second molecule is also the ligand bound to the macromolecule. Claim 33 has been amended at step (b) to recite that the second sample contains the macromolecule, the second molecule and a ligand, which clearly indicates that the second sample contains three components and that the second molecule and ligand are distinct. Claims 38 and 44 already recite in step (b) that the second sample contains three components, the macromolecule, the second molecule and a ligand or a second ligand, respectively. Accordingly, it is respectfully submitted that these claims are clear and definite.

Claims 38-49 are alleged to be indefinite for the term “alternatively” in that it is allegedly unclear whether the second molecule and second ligand associate with the macromolecule at the same time or at the same place on the macromolecule. Claims 38 and 44 have been amended to delete the phrase containing the term “alternatively.” Furthermore, the specification teaches that a method can be used to identify an exposed position in a molecule that binds the ligand (page 26, lines 13-28). As illustrated in Figures 5A and 5B and described on page 26, a macromolecule contains protons that are exposed to the second molecule and can exchange with protons of the second molecule (page 26, lines 13-18, and Figure 5A). A ligand that binds the macromolecule precludes the simultaneous binding of the second molecule at the same site and thereby results in perturbations compared to the macromolecule without the ligand bound (page 26, lines 20-28, and

Figure 5B). The second molecule and ligand are described as “alternatively” associating with and dissociating from the macromolecule, as do all molecules that bind to each other non-covalently (page 27, lines 21-29). Applicants respectfully submit, based on the teachings in the specification, that one skilled in the art would readily understand the meaning of these claims.

#### Rejections Under 35 U.S.C. § 102

The rejection of claims 1, 2, 6, 13, 14, 18-25, 27-29 and 32-49 under 35 U.S.C. § 102(e) as allegedly anticipated by Sem, U.S. Patent No. 6,333,149, is respectfully traversed. Without addressing the merits of the rejections set forth in the Office Action, Applicants have nevertheless amended claim 1 to incorporate the language of dependent claim 15, which has not been rejected over this reference, and reserve the right to pursue the claims as originally filed without prejudice in a related application. In light of the incorporation of the limitations of claim 15 into claim 1, it is respectfully submitted that this rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

#### Rejections Under 35 U.S.C. § 102 or 103

The rejection of claims 1-6, 13, 14, 18-25, 27, 29 and 33-35 under 35 U.S.C. § 102(b) as allegedly anticipated by Fesik et al., U.S. Patent No. 5,804,390, in light of Bax et al., Acc. Chem. Res. 26:131-138 (1993), or under 35 U.S.C. § 103 as allegedly obvious over Fesik et al. in light of Bax et al., is respectfully traversed. Without addressing the merits of the rejections set forth in the Office Action, Applicants have nevertheless amended claim 1 to incorporate the language of dependent claim 15, which has not been rejected over these references, and reserve the right to pursue the claims as originally filed without prejudice in a related application. In light of the incorporation of the limitations of claim 15 into claim 1, it is respectfully submitted that this rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 7-10 under 35 U.S.C. § 103 as allegedly obvious over Fesik et al., *supra*, in view of Bax et al., *supra*, is respectfully traversed. Without addressing the merits of the rejections set forth in the Office Action, Applicants have nevertheless amended claim 1 to

incorporate the language of dependent claim 15, which has not been rejected over these references, and reserve the right to pursue the claims as originally filed without prejudice in a related application. In light of the incorporation of the limitations of claim 15 into claim 1, it is respectfully submitted that this rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 12 and 26 under 35 U.S.C. § 103 as allegedly obvious over Fesik et al., *supra*, in view of Bax et al., *supra*, and further in view of Ohno et al., J. Mol. Biol. 282:421-423 (1998), is respectfully traversed. Without addressing the merits of the rejections set forth in the Office Action, Applicants have nevertheless amended claim 1 to incorporate the language of dependent claim 15, which has not been rejected over these references, and reserve the right to pursue the claims as originally filed without prejudice in a related application. In light of the incorporation of the limitations of claim 15 into claim 1, it is respectfully submitted that this rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claim 11 under 35 U.S.C. § 103 as allegedly obvious over Fesik et al., *supra*, in view of Bax et al., *supra*, and further in view of Xu et al., J. Am. Chem. Soc. 118:9176-9177 (1996), is respectfully traversed. Without addressing the merits of the rejections set forth in the Office Action, Applicants have nevertheless amended claim 1 to incorporate the language of dependent claim 15, which has not been rejected over these references, and reserve the right to pursue this claim as originally filed without prejudice in a related application. In light of the incorporation of the limitations of claim 15 into claim 1, it is respectfully submitted that this rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claim 16 under 35 U.S.C. § 103 as allegedly obvious over Fesik et al., *supra*, in view of Bax et al., *supra*, and further in view of Pervushin et al., U.S. Patent No. 6,133,736, is respectfully traversed. Without addressing the merits of the rejections set forth in the Office Action, Applicants have nevertheless amended claim 1 to incorporate the language of dependent claim 15, which has not been rejected over these references, and reserve the right to

pursue this claim as originally filed without prejudice in a related application. In light of the incorporation of the limitations of claim 15 into claim 1, it is respectfully submitted that this rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 39 and 45 under 35 U.S.C. § 103 as allegedly obvious over Sem et al., U.S. Patent No. 6,333,149, is respectfully traversed. Without addressing the merits of the rejections set forth in the Office Action, Applicants have nevertheless amended claim 1 to incorporate the language of dependent claim 15, which has not been rejected over this reference, and reserve the right to pursue the claims as originally filed without prejudice in a related application. In light of the incorporation of the limitations of claim 15 into claim 1, it is respectfully submitted that this rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

#### Double Patenting

The rejection of claims 1-6, 13, 22-25, 27-31 and 33-37 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-8, 13 and 25-31 of U.S. Patent No. 6,333,149, is respectfully traversed. Without addressing the merits of the rejections set forth in the Office Action, Applicants have nevertheless amended claim 1 to incorporate the language of dependent claim 15, which has not been rejected over this reference. In light of the incorporation of the limitations of claim 15 into claim 1, it is respectfully submitted that this rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 1-6, 13, 22-25, 27-31 and 33-37 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 2, 8, 14-26, 34, 36, 37, 40, 43, 44 and 46 of U.S. Patent No. 6,620,589, is respectfully traversed. Without addressing the merits of the rejections set forth in the Office Action, Applicants have nevertheless amended claim 1 to incorporate the language of dependent claim 15, which has not been rejected over this reference, and reserve the right to pursue the claims as originally filed without prejudice in a related application. In light of the incorporation of the limitations of claim 15 into claim 1, it is respectfully

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submitted that this rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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